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(FILE 'HOME' ENTERED AT 16:44:58 ON 06 OCT 2003)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
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L1	1215 S LDL AND PROTEASE?
L2	6 S L1 AND TAIL?
L3	4 DUPLICATE REMOVE L2 (2 DUPLICATES REMOVED)
L4	435 S LDL AND PROTEOLYSIS?
L5	163 DUPLICATE REMOVE L4 (272 DUPLICATES REMOVED)
L6	46 S L5 AND PROTEASE?
L7	46 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
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L9	16 S L4 AND REVIEW?
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L5 ANSWER 17 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 6
 AN 1998:484174 BIOSIS
 DN PREV199800484174
 TI **Presenilin-1** mutations associated with familial Alzheimer's
 disease do not disrupt protein transport from the endoplasmic reticulum to
 the Golgi apparatus.
 AU Tan, Yizheng; Hong, Jin; Doan, Tam; McConlogue, Lisa; Maltese, William A.
 (1)
 CS (1) Hood Res. Program, Weis Cent. Res., Pa. State Univ. Coll. Med., 100 N.
 Academy Ave., Danville, PA 17822-2616 USA
 SO Biochimica et Biophysica Acta, (July 1, 1998) Vol. 1407, No. 1, pp. 69-78.
 ISSN: 0006-3002.
 DT Article
 LA English
 AB Mutations in genes encoding **presenilin-1** (PS1) and
presenilin-2 (PS2) have been linked to familial forms of
 Alzheimer's disease (AD). Cells expressing mutant **presenilins**
 produce elevated levels of Abeta42, the major amyloid peptide found in AD
 plaques. The mechanism whereby this occurs remains unknown, but the
 localization of **presenilins** to endoplasmic reticulum (ER) and
 Golgi compartments has suggested that they may function in intracellular
 trafficking pathways involved in processing beta-amyloid precursor
 proteins (APP). To test this possibility, we coexpressed PS1(wt),
 PS1(M146L), or PS1(L286V) in HEK293 cells together with the **LDL**
receptor, a classic glycoprotein marker-that undergoes
 posttranslational O-glycosylation in the Golgi compartment. Pulse-chase
 analysis of the **receptor** indicated that mutant
presenilins had no effect on ER forward Golgi transport. Similar
 results were obtained when the studies were carried out with cells
 expressing the Swedish variant of APP (SWAPP751) instead of the
LDL receptor. Moreover, secretion of the soluble
 exodomain polypeptide fragments of SWAPP751 that arise from
 alpha-secretase and beta-secretase cleavage was not markedly affected by
 the PS1 mutants. Despite the lack of discernible effect of the PS1 mutants
 on trafficking of proteins through the Golgi apparatus, they caused a
 substantial increase in the proportion of Abeta42 relative to total AP in
 the culture medium. The results suggest that mutant forms of PS1 cause
 elevated production of Abeta42 by a mechanism that is independent of a
 major disruption of exocytic trafficking of APP.
 CC Nervous System - Pathology *20506
 Cytology and Cytochemistry - Human *02508
 Genetics and Cytogenetics - Human *03508
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 BC Hominidae 86215
 IT Major Concepts
 Genetics; Nervous System (Neural Coordination)
 IT Parts, Structures, & Systems of Organisms
 endoplasmic reticulum; Golgi apparatus
 IT Diseases
 familial Alzheimer's disease: genetic disease, nervous system disease
 IT Chemicals & Biochemicals
 beta-amyloid precursor protein; **presenilin-1**: mutation;
presenilin-2: mutation
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 HEK293 (Hominidae)
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:414226 CAPLUS
 DN 137:182782
 TI Proteolytic processing of low density lipoprotein receptor-related protein
 mediates regulated release of its intracellular domain
 AU May, Petra; Reddy, Y. Krishna; Herz, Joachim
 CS Department of Molecular Genetics, University of Texas Southwestern Medical
 Center, Dallas, TX, 75390, USA
 SO Journal of Biological Chemistry (2002), 277(21), 18736-18743
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 CC 13-2 (Mammalian Biochemistry)
 AB The low d. lipoprotein (LDL) receptor-related protein
 (LRP) is a multifunctional cell surface receptor that interacts through
 its cytoplasmic tail with adaptor and scaffold proteins that
 participate in cellular signaling. Its extracellular domain, like that of
 the signaling receptor Notch and of amyloid precursor protein (APP), is
 proteolytically processed at multiple positions. This similarity led us
 to investigate whether LRP, like APP and Notch, might also be cleaved at a
 third, intramembranous or cytoplasmic site, resulting in the release of
 its intracellular domain. Using independent exptl. approaches we
 demonstrate that the cytoplasmic domain is released by a
 .gamma.-secretase-like activity and that this event is modulated by
 protein kinase C. Furthermore, cytoplasmic adaptor proteins that bind to
 the LRP tail affect the subcellular localization of the free
 intracellular domain and may regulate putative signaling functions.
 Finally, we show that the degrdn. of the free tail fragment is
 mediated by the proteasome. These findings suggest a novel role for the
 intracellular domain of LRP that may involve the subcellular translocation
 of preassembled signaling complexes from the plasma membrane.
 ST LRP proteolysis secretase kinase C membrane signaling
 IT Biological transport
 (intracellular; proteolytic processing of low d. lipoprotein
 receptor-related protein mediates regulated release of its
 intracellular domain)
 IT Cell membrane
 Protein degradation
 (proteolytic processing of low d. lipoprotein receptor-related protein
 mediates regulated release of its intracellular domain)
 IT Receptors
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (.alpha.2-macroglobulin; proteolytic processing of low d. lipoprotein
 receptor-related protein mediates regulated release of its
 intracellular domain)
 IT 338454-52-7, .gamma.-Secretase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (proteolytic processing of LRP by .gamma.-secretase-like activity
 mediates regulated release of its intracellular domain)
 IT 141436-78-4, Protein kinase C
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (proteolytic processing of low d. lipoprotein receptor-related protein
 is modulated by protein kinase C)
 RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
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